

Dayhoff sequences, SPBC16H5_5, S64705, YAL5_SCHPO, CYP4_CAEEL, CELC34D4_7, CYPA_CAEEL, HUMORF006_1, CYPI_MYCTU, AF043642_1 and HSSRCYP_1.

EXAMPLE 41: Isolation of cDNA Clones Encoding Human PRO873

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA39621. Based on the DNA39621 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO873.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-AGGTGCCTGCAGGAGTCCTGGGG-3' (SEQ ID NO:255)

reverse PCR primer 5'-CCACCTCAGGAAGCCGAAGATGCC-3' (SEQ ID NO:256)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA39621 sequence which had the following nucleotide sequence:

hybridization probe

5'-GAACGGTACAAGTGGCTGCGCTTCAGCGAGGACTGTCTGTACCTG-3' (SEQ ID NO:257)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO873 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver tissue (LIB229).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO873 [herein designated as UNQ440 (DNA44179-1362)] (SEQ ID NO:253) and the derived protein sequence for PRO873.

The entire nucleotide sequence of UNQ440 (DNA44179-1362) is shown in Figure 90 (SEQ ID NO:253). Clone UNQ440 (DNA44179-1362) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 139-141 and ending at the stop codon at nucleotide positions 1774-1776 (Figure 90). The predicted polypeptide precursor is 545 amino acids long (Figure 91). The full-length PRO873 protein shown in Figure 91 has an estimated molecular weight of about 58,934 daltons and a pI of about 9.45. Analysis of the full-length PRO873 sequence shown in Figure 91 (SEQ ID NO:254) evidences the presence of the following features: a signal peptide from about amino acid 1 to about amino acid 29; a carboxylesterase type-B serine active site at about amino acid 312 to about amino acid 327; a carboxylesterase type-B signature 2 motif at about amino acid 218 to about amino acid 228; and three potential N-glycosylation sites at about amino acid 318 to about amino acid 321, about amino acid 380 to about amino acid 383, and about amino acid 465 to about amino acid 468. Clone UNQ440 (DNA44179-1362) has been deposited with ATCC on May 6, 1998 and is assigned ATCC deposit no. 209851.

Analysis of the amino acid sequence of the full-length PRO873 polypeptide suggests that it possesses significant sequence similarity to a human liver carboxylesterase, thereby indicating that PRO873 may be a novel carboxylesterase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO873 amino acid sequence and the following Dayhoff sequences:

ES10_RAT, GEN12405, AB010633_1, EST4_RAT, A48809, SASB_ANAPL, RNU41662_1, RNU22952_1, BAL_RAT, GEN13522.

EXAMPLE 42: Isolation of cDNA Clones Encoding Human PRO940

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA47442. Based on the DNA47442 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO940.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CAAAGCCTGCGCCTGGTCTGTG-3' (SEQ ID NO:260)

reverse PCR primer 5'-TTCTGGAGCCAGAGGGTGCTGAG-3' (SEQ ID NO:262)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47442 sequence which had the following nucleotide sequence

hybridization probe

5'-GGAGCTGCCACCCATTCAAATGGAGCACGAAGGAGAGTTCACCTG-3' (SEQ ID NO:263)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO940 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver tissue (LIB229).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO940 [herein designated as UNQ477 (DNA54002-1367)] (SEQ ID NO:258) and the derived protein sequence for PRO940.

The entire nucleotide sequence of UNQ477 (DNA54002-1367) is shown in Figure 92 (SEQ ID NO:258). Clone UNQ477 (DNA54002-1367) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 46-48 and ending at the stop codon at nucleotide positions 1678-1680 (Figure 92). The predicted polypeptide precursor is 544 amino acids long (Figure 93). The full-length PRO940 protein shown in Figure 93 has an estimated molecular weight of about 60,268 daltons and a pI of about 9.53. Analysis of the full-length PRO940 sequence shown in Figure 93 (SEQ ID NO:259) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15, potential N-glycosylation sites from about amino acid 100 to about amino acid 103, from about amino acid 297 to about amino acid 300 and from about amino acid 306 to about amino acid 309 and an immunoglobulin and major histocompatibility complex signature sequence block from about amino acid 365 to about amino acid 371. Clone UNQ477 (DNA54002-1367) has been deposited with ATCC on April 7, 1998 and is assigned ATCC deposit no. 209754.

Analysis of the amino acid sequence of the full-length PRO940 polypeptide suggests that it possesses significant sequence similarity to CD33 and the OB binding protein-2. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO940 amino acid sequence and the following Dayhoff sequences, CD33_HUMAN, HSU71382_1, HSU71383_1, D86359_1, PGBM_HUMAN, MAGS_MOUSE, D86983_1, C22B_HUMAN, P_W01002 and HVU24116_1.

EXAMPLE 43: Isolation of cDNA Clones Encoding Human PRO941

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA35941. An EST sequence proprietary to Genentech was employed in the assembly and is herein designated DNA6415 (Figure 96; SEQ ID NO:265). Based on the DNA35941 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO941.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTTGACTGTCTCTGAATCTGCACCC-3' (SEQ ID NO:266)

reverse PCR primer 5'-AAGTGGTGAAGCCTCCAGTGTGG-3' (SEQ ID NO:267)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35941 sequence which had the following nucleotide sequence

hybridization probe

5'-CCACTACGGTATTAGAGCAAAAGTTAAAAACCATCATGGTTCCTGGAGCAGC-3' (SEQ ID NO:268)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO941 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO941 [herein designated as UNQ478 (DNA53906-1368)] (SEQ ID NO:263) and the derived protein sequence for PRO941.

The entire nucleotide sequence of UNQ478 (DNA53906-1368) is shown in Figure 94 (SEQ ID NO:263). Clone UNQ478 (DNA53906-1368) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 37-39 and ending at the stop codon at nucleotide positions 2353-2355 (Figure 94). The predicted polypeptide precursor is 772 amino acids long (Figure 95). The full-length PRO941 protein shown in Figure 95 has an estimated molecular weight of about 87,002 daltons and a pI of about 4.64. Analysis of the full-length PRO941 sequence shown in Figure 95 (SEQ ID NO:264) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 21, potential N-glycosylation sites from about amino acid 57 to about amino acid 60, from about amino acid 74 to about amino acid 77, from about amino acid 419 to about amino acid 422, from about amino acid 437 to about amino acid 440, from about amino acid 508 to about amino acid 511, from about amino acid 515 to about amino acid 518, from about amino acid 516 to about amino acid 519 and from about amino acid 534 to about amino acid 537, and cadherin extracellular repeated domain signature sequences from about amino acid 136 to about amino acid 146 and from about amino acid 244 to about amino acid 254. Clone UNQ478 (DNA53906-1368) has been deposited with ATCC on April 7, 1998 and is assigned ATCC deposit no. 209747.

Analysis of the amino acid sequence of the full-length PRO941 polypeptide suggests that it possesses significant sequence similarity to a cadherin protein, thereby indicating that PRO941 may be a novel cadherin protein family member. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO941 amino acid sequence and the following Dayhoff sequences,